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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,340	12/10/2001	Bernard Dubreucq	065691-0262	3890

22428 7590 04/06/2006

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EXAMINER	
BAUSCH, SARAE L	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 04/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,340	DUBREUCQ ET AL.	
	Examiner	Art Unit	
	Sarae Bausch	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 7-24* is/are pending in the application.

4a) Of the above claim(s) *7-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claim 1 is pending in the instant application. Claims 2-6 have been canceled. Claims 1 has been amended while claims 7-24 are withdrawn. This action is written in response to applicant's correspondence submitted 01/17/2006. All the amendments and arguments have been thoroughly reviewed but were found insufficient to place the instantly examined claims in condition for allowance. The following rejections are either newly presented, as necessitated by amendment, or are reiterated from the previous office action. Any rejections not reiterated in this action have been withdrawn as necessitated by applicant's amendments to the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is Final.**

Withdrawn Rejections

2. The rejections of claim 1 , under 35 U.S.C. 101, made in section 3 of the previous office action, is withdrawn in view of the amendment to the claims.

3. The rejections of claim 1, under 35 U.S.C. 112, first paragraph made in section 7 of the previous office action, is withdrawn in view of the amendment to the claims.

4. The rejections of claim 1, under 35 U.S.C. 102 (b), made in section 11-13 of the previous office action, is withdrawn in view of the amendment to the claims.

New Grounds of Rejection

Claim Rejections - 35 USC § 112- Enablement

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection was previously present in section 8 of the office action mailed 07/27/2005 and has been re-written to accommodate the amendment to claim 1.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

<u>The nature of the invention and the breadth of the claims</u>

Claim 1 is drawn to an isolated promoter sequence that allows expression of a gene of interest in the tissues of a plant, except in the maturing seed and in the dry seed consisting of SEQ ID No. 1. However, as will be further discussed, the specification does not enable one of skill in the art to generate a promoter sequence that is capable of expressing a gene of interest in the tissues of a plant except in the maturing seed and in the dry seed. The specification does not enable the claimed invention due to the limitation of "expression of a gene of interest in the tissue of plant, except in the maturing seed and in the dry seed".

Guidance in the Specification

While the specification does teach the sequence of a promoter, SEQ ID No. 1 and the gene expressed by this promoter, SEQ ID No. 5 and the protein that encodes the gene, SEQ ID No. 4, the specification provides no evidence of how to make or use SEQ ID No. 1 that are capable of functioning as a promoter to express any gene of interest in the tissues of a plant except in the maturing seed and in the dry seed. The specification merely discloses the sequence and structural information for the promoter encompassed in SEQ ID No. 1 and recites that the invention relates to the use of a portion of the sequence SEQ ID No. 1 for identifying fragments capable of promoting the expression of a gene of interest in a plant except in the seed (page 5, lines 1-8). The specification recites that the promoter may be modified by adding sequence such as enhancers, and/or by deleting nonessential and/or undesired regions (see page 5, lines 5-11), however the specification gives no guidance as to what sequences can be added or deleted, what portion of the sequence is essential, nonessential or required for promoter activity to allow for the expression of a gene in the tissue of a plant except in the maturing seed and in the dry seed.

The unpredictability of the art and the state of the prior art

The ability of a promoter to function is highly sequence specific. The art teaches repeatedly that mutations in a critical region of a promoter element can destroy the ability of a construct to function in promotion. For example, Pietrzkowski *et al.* (Experimental Cell Research, 193, 283-290 (1991)) teaches that when synthetic promoters were produced wherein the sequence of an enhancer element was mutated, little to no promotion was observed from the constructs where the promoter was mutated (see for example Figure 6). Chan *et al.* (Plant Molecular Biology 46 :131-141, (2001)) mutation in a critical XXIII element of the GAPB promoter abolished transcription completely (Figure 6), while mutations in other elements did not abolish activity (Figure 6). Thus, it is evident that it is highly unpredictable how promoter elements will respond to even very minor sequences changes. In addition, the order that promoter elements occur in a construct has an effect on the functionality of the promoter. Omilli *et al.* (Molecular and Cellular Biology, June 1986, p. 1875-1885) teach that the relative arrangement of promoter elements is a critical factor contributing to the activity of the promoter (ABSTRACT, for example).

Furthermore, Ruegger et al. teach the FAH1 gene encodes F5H, a Cyt P450-dependent monoxygenase required for the synthesis of sinapate esters and sinapic-derived syringe lignin (FAH1, F5H is the gene that SEQ ID No. 1 regulates) (see page 102, 1st column, 1st paragraph). Ruegger et al. teach that 630 bp of 3' DNA is sufficient for expression and mRNA stability in leaves when F5H is driven with a heterologous promoter but in vegetative tissue F5H expression requires addition downstream DNA in the context of its own promoter. Ruegger et al. teach that these data conclude that an element downstream of the DNA functions as a positive regulator of gene expression (see page 106, 2nd column, last paragraph). Ruegger et al. teach that the 3'

flanking DNA is not required for F5H expression in embryos but is required for adult tissues (see page 108, 2nd column, 3rd full paragraph). Ruegger et al. teaches F5H expression involves a regulatory element located 3' of its stop codon (see page 107, 1st column, 1st full paragraph). Ruegger et al. teach that the requirement for 3' flanking sequences in F5H expression further differentiates the regulation of F5H from that of other phenylpropanoid genes and the regulatory factors that control F5H expression in Arabidopsis may be independent of those that control upstream genes (See page 108, 2nd column, last paragraph cont'd to page 109). Ruegger et al. teach that results indicate that the 3' DNA is required for expression of an F5H promoter-driven GUS reporter gene in leaves and stems of adult plants but is not required for expression in embryos (see page 109, 1st column, 1st full paragraph). The GenBank accession number AC003096 teaches the nucleic acid sequence at positions 6867-7798, which is located 3' downstream from the fatty acid hydroxylase gene and comprises the sequence of instant SEQ ID No. 1. The GenBank accession number AC003096 teaches the coding region for fatty acid hydroxylase (FAH1) (the gene SEQ ID No. 1 regulates) is at positions 4397 to 6665 and the next coding region on the chromosome is gene At2g34750 at position 8739 to 12082.

Ruegger et al. teach that both the promoter for FAH1 (F5H) gene and the 3' downstream regulatory elements of the FAH1 gene are necessary for gene expression of FAH1. Alignment data shows that SEQ ID No. 1 is part of the 3' regulatory region of the FAH1 gene. Therefore, based on the teaching by Ruegger et al., SEQ ID No. 1 would not function as a promoter alone, or allow for expression of a gene of interest in the tissue of a plant except the maturing seed and in the dry seed. Ruegger et al. teach that 3' flanking region of the FAH1 gene (which comprises SEQ ID No.1) in addition with the FAH1 promoter shows expression in adult plants but not

embryos and further teaches expression in FAH1 gene by 3' regulatory region in seedlings (See figure 3). Therefore, based on the teachings in the prior art, it is unpredictable to isolate promoter sequence that would allow for expression of a gene of interest in the tissue of a plant but not in the maturing seed or dry seed.

Working Examples

On page 16, the specification provides an example of amplification of SEQ ID No. 1 by PCR using primers and identification of a putative TATA box at –100 bp from the presumed transcription site and a CCAAT box at –190 bp from the transcription start site. The specification describes cloning the PCR fragment into the construct pGEM-T vector and introducing this vector into a binary vector comprising the GUS reporter gene without a promoter and transforming the vector into planta (see page 16, lines 14-20). The specification asserts that there were thirteen primary transformant that were obtained and were tested for their GUS activity during development. The specification asserts that expression is strong from 20 hours after the start of soaking in the embryos and during development the expression is strong in all tissues (see page 16, lines 25-28). The specification asserts that these results demonstrate that the isolated promoter sequence indeed confers a very specific expression profile on the reporter gene used and the promoter is active throughout the development of the plant, in all tissues tested except in the seed of undergoing maturation (see page 16, lines 30-36). The specification asserts that the marker confirms functionality of the promoter and its specificity (see page 17, lines 1-2). However, the specification provides no control experiments of the

plasmid construct without a promoter sequence to determine of the GUS gene expression is due to the specific promoter.

Further, the specification provides no working examples of which portion of the promoter is necessary for expression of a gene. The specification is merely prophetic for determining the sequence of the promoter that is necessary for expression of a gene. The specification merely recites, on page 5, lines 1-10, that is may be possible to define the minimum region of the sequence of the promoter of the FAH gene for ensuring effective expression and the promoter may be modified by adding sequences such as enhancers and/or deletions of nonessential and/or undesirable regions. However, the specification does not give any guidance or working examples of which region of the promoter may be modified, deleted, or mutated and still maintain function as a promoter and specifically a promoter that is capable of expressing a gene in all tissues, except in the seed maturation. The specification envisions hypothetical situations where modification of the promoter sequence is possible without changing the function. However, it is unclear how one of skill in the art would design the most appropriate promoter sequence to practice this preferred embodiment of expressing a gene in all tissues, except in the seed maturation of a plant and furthermore, how one would determine the efficacy of the results of the embodiments as the specification does not teach a control experiment.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Quantity of Experimentation

Given the lack of guidance in the specification with regard to which sequences could be modified or which portion of the sequence of the promoter of SEQ ID No. 1 is required for promoter activity, the quantity of experimentation in this area is extremely large and undue. The skilled artisan would have to determine which nucleic acid residues, mutants, variants, and/or fragments would be capable of expressing a gene of interest in all tissues, except in the seed maturation of a plant. To practice the invention as broadly as it is claimed, the skilled artisan would have to construct and screen hundreds of millions of possible promoters that comprise encompasses variants, mutants, and homologs of SEQ ID NO 1 or any FAH gene from Arabidopsis, that would be capable of expressing a gene of interest in all tissue in a plant but not in the maturing seed and in the dry seed. The construction and screening of all of these possible promoters to determine the functional promoters would require undue experimentation because there is no way to predict which promoters would be functional given that promoter sequences are highly variable. The skilled artisan would have to perform an extremely large amount of trial and error analysis in a large study to determine if the promoter is in fact expressing a gene in all tissue except maturing seed and dry seed. This would require a large amount of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps. Thus given the broad claims in an art whose nature is identified as unpredictable, the lack of guidance on how to make a promoter that comprises mutants, variants, and homologs capable of expressing a gene of interest in all tissues of a plant except maturing seed and dry seed, the large quantity of research required to define the lack of guidance provided in the specification, the absence of working examples, and the negative teaching in the prior art balanced only against the high level of skill in the art, it is

the position of the examiner that it would require undue experimentation for one of skill in the art to make the claimed invention.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ruegger et al. (Plant Physiology 1999, 119:101-110) in view of GenBank accession number AC003096 (gi 2598082, Nov. 7, 1997).

It is noted that the claim is drawn to an isolated promoter, which allows for the

expression of a gene of interest in the tissues of a plant, except in the maturing seed and in the dry seed consisting of SEQ ID No. 1. The recitation of "expression of a gene of interest in the tissues of a plant except in the maturing seed and in the dry seed" is an intended use of the composition and the intended use of the composition has not been given patentable weight as it applies to this rejection.

Ruegger et al. teach the FAH1 gene encodes F5H, a Cyt P450-dependent monoxygenase required for the synthesis of sinapate esters and sinapic-derived syringe lignin (FAH1, F5H is the gene that SEQ ID No. 1 regulates) (see page 102, 1st column, 1st paragraph). Ruegger et al. teach F5H expression is dependent on a regulatory domain that is located 3' of the F5H stop codon, where its expression in embryos is independent of this downstream element (see page 102, 2nd column, last paragraph). Ruegger et al. teach genomic Arabidopsis DNA carrying the F5H coding sequence and the 5' and 3' regulatory regions (see page 102, 2nd column, last sentence). Ruegger et al. teach that 630 bp of 3' DNA is sufficient for expression and mRNA stability in leaves when F5H is driven with a heterologous promoter but in vegetative tissue F5H expression requires addition downstream DNA in the context of its own promoter. Ruegger et al. teach that these data conclude that an element downstream of the DNA functions as a positive regulator of gene expression (see page 106, 2nd column, last paragraph). Ruegger et al. teach that the 3' flanking DNA is not required for F5H expression in embryos but is required for adult tissues (see page 108, 2nd column, 3rd full paragraph). Ruegger et al. teaches F5H expression involves a regulatory element located 3' of its stop codon (see page 107, 1st column, 1st full paragraph). Ruegger et al. teach that the requirement for 3' flanking sequences in F5H expression further differentiates the regulation of F5H from that of other phenylpropanoid genes and the regulatory

factors that control F5H expression in Arabidopsis may be independent of those that control upstream genes (See page 108, 2nd column, last paragraph cont'd to page 109). Ruegger et al. teach that results indicate that the 3' DNA is required for expression of an F5H promoter-driven GUS reporter gene in leaves and stems of adult plants but is not required for expression in embryos (see page 109, 1st column, 1st full paragraph). Ruegger et al. does not teach an isolated promoter that consists of SEQ ID No. 1

The GenBank accession number AC003096 teaches the nucleic acid sequence at positions 6867-7798, which is located 3' downstream from the fatty acid hydroxylase gene and comprises the sequence of instant SEQ ID No. 1. The GenBank accession number AC003096 teaches the coding region for fatty acid hydroxylase (FAH1) (the gene SEQ ID No. 1 regulates) is at positions 4397 to 6665 and the next coding region on the chromosome is gene At2g34750 at position 8739 to 12082.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the sequences taught by Ruegger et al. to include sequences that encompass the 3' regulatory region of the F5H gene taught by GenBank Accession number. The ordinary artisan would have been motivated to include multiple different lengths of nucleotides that would encompass the regulatory region of the 3' region downstream of the F5H gene to determine the involvement of the 3' flanking DNA in plant gene expression as taught by Ruegger and GenBank accession number AC003096. The ordinary artisan would have had a reasonable expectation of success that a sequence consisting of 6867-7798 would regulate the expression of F5H because Ruegger et al. teaches that the 3' flanking DNA is necessary for F5H expression in adult tissue and further teaches that 630 bp of 3' DNA

is sufficient for expression and mRNA stability in leaves when F5H is driven with a heterologous promoter but in vegetative tissue F5H expression requires addition downstream DNA in the context of its own promoter. Determining regulatory regions within genomic DNA is routine experimentation and the ordinary artisan would have been motivated to generate a number of different sequences of the 3' regulatory region of the F5H gene as taught by Ruegger, including sequences that consist of positions 6867-7798 as taught by the GenBank Accession number. These sequences are considered functionally equivalent, absent secondary considerations.

Conclusion

8. No claims are allowable.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarae Bausch whose telephone number is (571) 272-2912. The examiner can normally be reached on M-F 10am-7pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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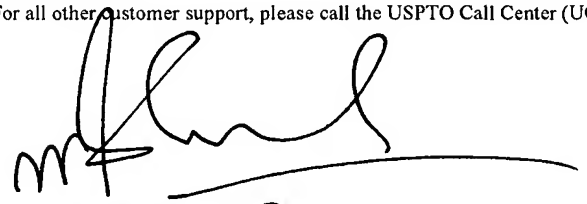

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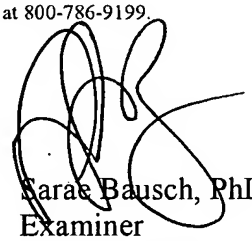

Sarae Bausch, PhD.
Examiner
Art Unit 1634